INNO-BIA PLASMA Aß FORMS

A multiparameter bead-based immunoassay for the simultaneous quantification of human ß-amyloid (Aß) forms $Aß_{1-42}$, $Aß_{1-40}$, $Aß_{N-42}$, and $Aß_{N-40}$ in plasma using xMAP® technology.*

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Standardized quantification of ß-amyloid isoforms

in blood

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Results with home-brew plasma assays cannot be easily compared.

Differences between studies may be related to:
study design / patient selection / and test variability.

Name	n	Duration	Population	Results
van Dijk et al. [1]	1077	NA	60 – 90 years dementia-free	$A\beta_{1-42}$ and $A\beta_{1-40}$ increased in subjects with white matter lesions/lacunar infarcts assoc. with APOE epsilon4 allele
Mayeux et al. [2]	530	3 years	> 65 years	$A\beta_{1-42}$ and $A\beta_{1-40}$ increase with age
Schupf et al. [3]	172	NA	108 Down's 64 controls	$A\beta_{1-42}$ and $A\beta_{1-40}$ increased in Down's vs controls $A\beta_{1-42}$ higher in Down's carrying APOE epsilon4 allele
Scheuner et al. [4]	216	NA	120 controls 96 FAD mutations	FAD-linked mutations increase $A\beta_{1-42}$ levels
Assini et al. [5]	160	NA	88 MCI patients 72 controls	Higher $A\beta_{1-42}$ in women with MCI vs men with MCI or controls
Watson et al. [6]	30	6 months	30 patients with either MCI or AD	6-month pilot study of PPAR-γ agonist rosiglitazone: no change in $A\beta_{1-42}$ or $A\beta_{1-40}$ levels in patients on drug (n=20) vs decrease in patients on placebo (n=10)

Table 1. Selected 'baseline' studies of plasma $A\beta_{1-42}$ and/or $A\beta_{1-40}$

Results from many studies in plasma are contradictory.

Factors influencing Aß plasma levels may include:
gender, age, concomitant medication, duration and type of neurodegenerative disease, the stage at which blood is sampled.

Name	n	Duration	Population	Results
Mayeux et al. [2]	530	3 years	> 65 years	$A\beta_{1-42}$ and $A\beta_{1-40}$ increase with age In AD, initially higher $A\beta_{1-42}$ and $A\beta_{1-40}$, but later decline if AD, highest $A\beta_{1-42}$ in patients who died
Blasko et al. [7]	526	> 2 years	75 years	Insulin and biguanides increase $A\beta_{1-42}$ levels *Gingko biloba* and NSAIDs decrease $A\beta_{1-42}$ levels Long-term drug use may influence $A\beta_{1-42}$ levels
Sobow et al. [8]	128	NA	35 controls 39 MCI 54 AD	In AD and controls, no changes in $A\beta_{1-42}$ and $A\beta_{1-40}$ In MCI, only $A\beta_{1-42}$ higher vs AD and controls In MCI, lower $A\beta_{1-40}/A\beta_{1-42}$ ratio vs AD or controls
Van Oijen et al. [9]	1756	> 8.6 years	Mean 68.6 y	At baseline, higher Aβ40 = higher risk for dementia In dementia, higher $A\beta_{1-40}$, lower $A\beta_{1-42}$ In dementia, lower $A\beta_{1-42}/A\beta_{1-40}$ ratio
Graff-Radford et al. [10]	563	2 – 12 years	Mean 78 y	MCI or AD patients had lower $A\beta_{1-42}/A\beta_{1-40}$ ratios Use of only $A\beta_{1-42}$ or $A\beta_{1-40}$ alone insufficient
Blasko et al. [11]	487	2.5 years	75 years	Increase of plasma $A\beta_{1-42}$ initial AD event reflecting transition from cognitive health to AD; Aβ42 alone not suitable as biomarker

Table 2. Larger studies of plasma $A\beta_{1-42}$ and $A\beta_{1-40}$

References. 1. van Dijk EJ, Prins ND, Vermeer SE, Hofman A, van Duijn CM, Koudstaal PJ, et al. Ann Neurol 2004;55:570-575. **2.** Mayeux R, Honig LS, Tang MX, Manly J, Stern Y, Schupf N, et al. Neurology 2003;61:1185-1190. **3.** Schupf N, Patel B, Silverman W, Zigman WB, Zhong N, Tycko B, et al. Neurosci Lett 2001;301:199-203. **4.** Scheuner D, Eckman C, Jensen M, Song X, Citron M, Suzuki N, et al. Nat Med 1996;2:864-870. **5.** Assini A, Cammarata S, Vitali A, Colucci M, Giliberto L, Borghi R, et al. Neurology 2004;63:828-831. **6.** Watson GS, Cholerton BA, Reger MA, Baker LD, Plymate SR, Asthana S, et al. Am J Geriatr Psychiatry 2005;13:950-958. **7.** Blasko I, Kemmler G, Krampla W, Jungwirth S, Wichart I, Jellinger K, et al. Neurobiol Ageing 2005;26:1135-1143. **8.** Sobow T, Flirski M, Kloszewska I, Liberski PP. Acta Neurobiol Exp (Wars) 2005;65:117-124. **9.** Van Oijen M, Hofman A, Soares HD, Koudstaal PJ, Breteler MMB. Lancet Neurol 2006;5:655-660. **10.** Graff-Radford NR, Crook JE, Lucas J, Boeve BF, Knopman DS, Ivnik RJ, et al. [personal communication]. **11.** Blasko I, Jellinger K, Kemmler G, Krampla W, Jungwirth S, Wichart I, et al. Neurobiology of Aging 2007;28: In Press.

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The following types of studies could be useful to better elucidate the potential role of Aß isoforms in AD.

New prospects for research

- Defining normal intra-individual physiological changes in Aß isoforms over time, and according to gender
- Studies comparing levels of Aß isoforms between healthy individuals over time
- Exploring changes in Aß isoforms over time in individuals developing MCI and AD, and their variations between individuals

- Exploring utility of different combinations of Aß isoforms as markers of MCI and AD
- Exploring utility of Aß isoforms as AD prognostic marker
- Exploring utility of Aß isoforms for differential diagnosis

The well-standardized INNO-BIA plasma Aß forms: a new starting point for research

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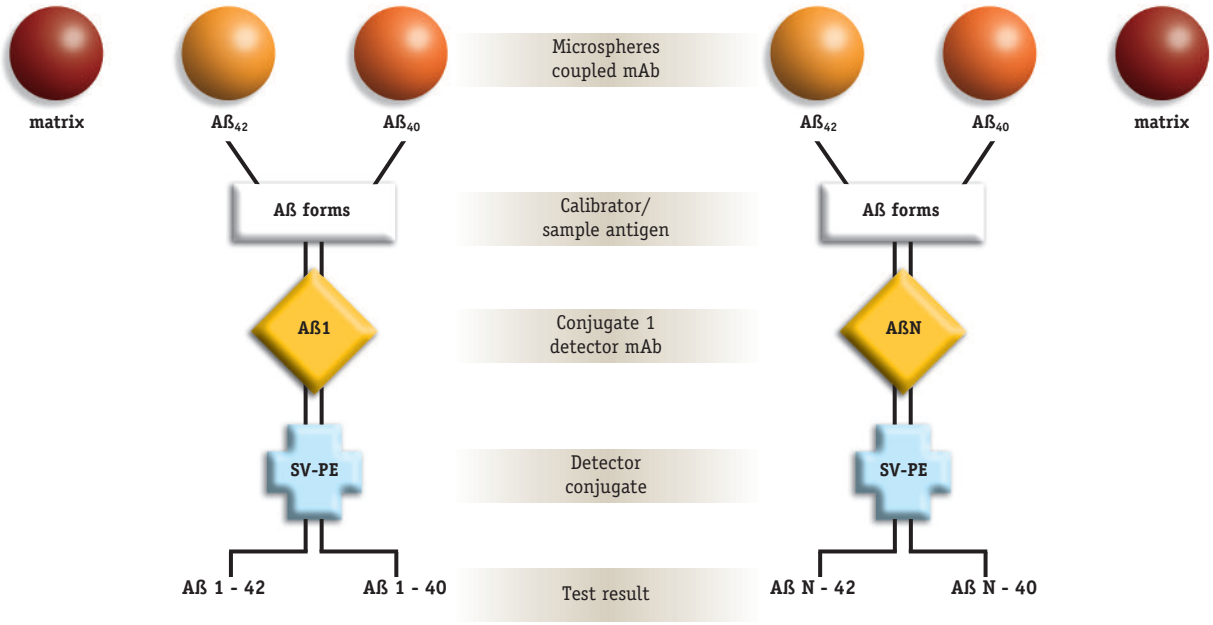
INNO-BIA plasma Aß forms

1 multiparameter kit, 2 modules, 4 biomarkers

MODULE A:
simultaneous quantification of $Aß_{1-42}$ and $Aß_{1-40}$

MODULE B:
simultaneous quantification of $Aß_{N-42}$ and $Aß_{N-40}$



- Each module with an internal control to verify for matrix interference(s)

Sequence of (human) ß-amyloid and epitopes of selected monoclonal antibodies

High performance using xMAP® technology*

- High analytical assay sensitivity
- Quantifying $Aß_{40}$ and $Aß_{42}$ in one well, which lowers test variability
- Low intra- and inter-assay variability, even at low concentrations
- High reproducibility
- Broad dynamic range

Ease of use

- Only one test procedure
- Six ready-to-use (multiparametric) standards
- Two run-validation (non-plasma) controls
- Limited number of handling steps
- Sample - EDTA-plasma
  - 1:3 diluted with plasma diluent
  - 25 µL plasma/well
  - duplicate testing

Presentation		art. no.
INNO-BIA plasma Aß forms	2 x 96 wells/kit	80933

Disclaimer. A license regarding Amyloid beta antibodies contained in this product under patents US 570349 and EP 0683234 has been obtained from Takeda Pharmaceutical Company Limited.
Furthermore, a license for the use of Amyloid beta monoclonal antibodies contained in this product under patents US 5,593,846A, US 5,766,846A, US 5,837,672A, US 6,284,221B1, US 6,610,493B1, US 5,441,870A, US 5,721,130A, US 5,605,811A and US 6,114,133A has been obtained from Eli Lilly and Company.

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